Interspecies organogenesis generates autologous functional islets.

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Public Summary:
One of the reasons for Diabetes is the pancreas not producing enough insulin. Islet transplantation is an established therapy for diabetes. We injected mouse pluripotent stem cells (PSCs) into a pancreas deficient rat blastocyst, and was able to generate rat sized pancreas compose of mouse PSCs. We transplanted these cells into mice with diabetes and was able to suppress the diabetes. This provides evidence for future therapies using PSC-derived islets generated by blastocyst complementation in a xenogeneic host.

Scientific Abstract:
Islet transplantation is an established therapy for diabetes. We have previously shown that rat pancreata can be created from rat pluripotent stem cells (PSCs) in mice through interspecies blastocyst complementation. Although they were functional and composed of rat-derived cells, the resulting pancreata were of mouse size, rendering them insufficient for isolating the numbers of islets required to treat diabetes in a rat model. Here, by performing the reverse experiment, injecting mouse PSCs into Pdx-1-deficient rat blastocysts, we generated rat-sized pancreata composed of mouse-PSC-derived cells. Islets subsequently prepared from these mouse-rat chimaeric pancreata were transplanted into mice with streptozotocin-induced diabetes. The transplanted islets successfully normalized and maintained host blood glucose levels for over 370 days in the absence of immunosuppression (excluding the first 5 days after transplant). These data provide proof-of-principle evidence for the therapeutic potential of PSC-derived islets generated by blastocyst complementation in a xenogeneic host.